REMARKS

The above-identified notice required that Applicants submit:

1) A substitute paper copy of the Sequence Listing;

2) A substitute computer readable form (CRF) copy of the paper Sequence Listing; and

3) A statement that the content of the paper Sequence Listing and the computer readable copies are the same and include no new matter.

In response, there is attached a substitute paper copy of the Sequence Listing, which, pursuant to 37 CFR § 1.823 (a) (1), is numbered independently of the numbering of the remainder of the application. The undersigned hereby certifies that the substitute paper copy of the Sequence Listing does not introduce new matter.

There is also attached a substitute computer readable form copy of the substitute paper Sequence Listing. The undersigned hereby certifies that the content of the substitute paper Sequence Listing and the substitute computer readable form copy is the same and includes no new matter.

Early and favorable action is earnestly solicited.

Respectfully submitted,

NORRIS McLAUGHLIN & MARCUS, P.A.

By _____
Kurt G. Briscoe
Reg. No. 33,141

220 East 42nd Street
30th Floor
New York, New York 10017
Phone: (212) 808-0700
Fax: (212) 808-0700

CERTIFICATE OF MAILING

I hereby certify that the foregoing Response to Communication Regarding the Sequence Listing and the attached Mark-Up Showing the Changes Made in the Specification and accompanying Copy of the Notice, Substitute Paper Sequence Listing (pages 1-7) and Computer Diskette are being deposited with the United States Postal Service as first class mail in an envelope addressed to: Hon. Commissioner of Patents, Washington, D.C. 20231, on the date indicated below:

Date: July 10, 2001

By _____
Kurt G. Briscoe
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MARK-UP SHOWING THE CHANGES MADE IN THE SPECIFICATION

Amend the paragraph at page 8, lines 10-22, to read as follows:

An expression plasmid encoding the aminoterminal fragment of urokinase plasminogen activator (u-PA), amino acids 1-138, hereafter referred to as ATF, can be constructed by deleting the DNA sequences encoding amino acids 139 till 401 in an expression plasmid for the full length u-PA using a polymerase chain reaction (PCR) with the following oligonucleotides: 5' - cccgggctttttttccatctgcgcagtc -3' **(SEQ ID NO.: 1)** and 5' - agggtcaccaaggaagagaatggc -3' **(SEQ ID NO.: 2)**. After amplification by PCR the newly formed DNA fragment can be circularized by ligation to restore the circular character of the expression plasmid. In this way an expression plasmid encoding the ATF and the C terminal last 11 amino acid residues including the stop codon can be constructed.

Amend the paragraph at page 8, line 34, through page 9, line 18, to read as follows:

DNA fragments encoding amino acid residues 36-93 of bovine pancreatic trypsin inhibitor (BPTI) and the homologous amino acid residues of bovine spleen trypsin inhibitor (BSTI) can be isolated by performing a PCR reaction on gnomic DNA isolated for bovine aortic endothelial cells using the following oligonucleotides: 5' - *tc*gcg*a*cctgacttctgcctagagc - 3' **(SEQ**

ID NO.: 3) covering nucleotides 2509 to 2533 (with modifications, indicated in *italics,* in the 5' region of the oligonucleotide to introduce a NruI site (underlined) for cloning purposes) of the BPTI gene according to the published sequence (GENBANK, BTBPTIG), and nucleotide 2442 to 2462 of the BSTI gene according to the published sequence (GENBANK, BTBSTIG) and 5' ggtc*acc*cagggccc*aatatt*accacc -3' **(SEQ ID NO.: 4)** covering nucleotides 2677 to 2704 of the BPTI gene and 2610 to 2636 of the BSTI gene (modified in the indicated nucleotide *(italics)* to introduce a BstEII and a SspI site respectively (underlined). The amplified DNA fragments then were cloned into an appropriate plasmid vector, pCRII or pUC13, and then the exact sequence of the amplified DNA fragments in the isolated clones was analyzed to differentiate between BPTI and BSTI which have a very high degree of homology.

Amend the paragraph at page 9, lines 21-32, to read as follows:

The DNA fragment encoding amino acids 1 to 207 of the human tissue inhibitor of metalloproteinase typ 1 is isolated by performing a reverse transcriptase polymerase chain reaction on total RNA isolated from human foreskin fibroblasts by using the following oligonucleotides 5' - agagagacaccagagaacccaccat - 3' **(SEQ ID NO.: 5)** covering nucleotide 41 to 65 of the human TIMP-1 cDNA (according to the sequence in GENBANK HSTIMPR) and 5' - tcattgt ccgaagaaagatgggag -3' **(SEQ ID NO.: 6)** covering nucleotides740 till 755. The amplified DNA fragment was cloned into an appropriate host vector, pUC13, and then the exact

sequence of the amplified DNA fragment in the isolated clones was analyzed.

Amend the paragraph at page 10, lines 18-30, to read as follows:

Starting from a pCRII plasmid in which a 1373 base pair fragment of the uPA cDNA was cloned, a PCR reaction with the oligonucleotides 5'- *ccc*gggctttttttccatctgcgcagtc - 3' **(SEQ ID NO.: 1)** (SmaI site underlined and nucleotides changed in *italics)* and 5' - agggtcaccaaggaagagaatggc -3' **(SEQ ID NO.: 2)** (BstEII site underlined and nucleotide changed in *italics)* was performed as described in example 1 to make a pCRII-ATF plasmid (see figure 1). Subsequently this pCRII-ATF plasmid was digested with the restriction enzymes SmaI and BsteII. In parallel the pCRII-BPTI plasmid was digested with the restriction enzymes NruI and BsteII and the BPTI containing fragment was cloned into the pCRII-ATF plasmid (see figure 2). The construction pCRII-ATF-BPTI is shown in Fig. 2.

Amend the paragraph at page 11, lines 23-29, to read as follows:

Starting from a pCRII plasmid in which a 1373 base pair fragment of the uPA cDNA was cloned, a PCR reaction with the oligonucleotides 5'-cccgggctttttttccatctgcgcagtc -3' **(SEQ ID NO.: 1)** and 5'-agggtcaccaaggaagagaatggc - 3' **(SEQ ID NO.: 2)** was performed as described in example 1 to make a pCRII-ATF plasmid (see figure 1). Subsequently this pCRII-ATF plasmid